HHS Public Access

Author manuscript

Epidemiology. Author manuscript; available in PMC 2019 November 01.

Published in final edited form as:

Epidemiology. 2018 November ; 29(6): 756–764. doi:10.1097/EDE.0000000000000910.

Vulnerability to the Cardiovascular Effects of Ambient Heat in Six U.S. Cities: Results from the Multi-Ethnic Study of Atherosclerosis (MESA)

Carina J. Gronlund[1], **Lianne Sheppard**[2], **Sara D. Adar**[1], **Marie S. O'Neill**[1,3], **Amy Auchincloss**[4], **Jaime Madrigano**[5], **Joel Kaufman**[2], and **Ana V. Diez Roux**[4]

[1]Epidemiology, University of Michigan School of Public Health, Ann Arbor, MI, USA

[2]Environmental and Occupational Health Sciences, University of Washington School of Public Health, Seattle, WA, USA

[3]Environmental Health Sciences, University of Michigan School of Public Health, Ann Arbor, MI, USA

[4]Epidemiology and Biostatistics, Drexel University Dornsife School of Public Health, Philadelphia, PA, USA

[5]RAND Corporation, Arlington, VA, USA

Abstract

Background: With climate change, temperatures are increasing. Heat-associated health events disproportionately affect certain subpopulations. However, prior research has often lacked information on individual-level health and air conditioning and neighborhood stressors/protections.

Objectives: To assess whether 1) heat (2-day mean temperature above local 75th percentiles) is associated with increased heart rate and decreased blood pressure, controlling for age, time, season, daily ozone, and daily particulate matter ($PM_{2.5}$), and 2) associations differ by anti-hypertensive-medication use, renal function, fasting glucose, emotional support, air conditioning ownership and use, normalized difference vegetation index, neighborhood safety, and residence-specific oxides of nitrogen and $PM_{2.5}$.

Methods: Health and behavioral characteristics were obtained repeatedly on participants of the Multi-Ethnic Study of Atherosclerosis in six U.S. sites (2000–2010). These were linked with airport temperature, air quality, and satellite- and survey-derived neighborhood characteristics. We used a fixed-effects design, regressing health outcomes on linear temperature splines with knots at

Corresponding Author: Carina Gronlund, PhD, MPH, Center for Social Epidemiology and Population Health, University of Michigan School of Public Health, 2663 SPH Tower, 1415 Washington Heights, Ann Arbor, MI 48109-2029, 734-615-9215 / gronlund@umich.edu.

Conflicts of Interest: The authors declare they have no actual or potential conflicts of interest.

Data availability: The computing code may be obtained from the corresponding author on request. The data may be obtained from the MESA Coordinating Center following completion of a Data Distribution Agreement and review and approval of a detailed proposal by MESA Publications and Steering Committees for soundness in science, methodology, and adherence to MESA policy.

the 75th percentiles, interaction terms for each characteristic, and adjustment for month-of-year, age, $PM_{2.5}$, and ozone.

Results: Overall, heat was not associated with heart rate. However, for a 2 degree-Celsius increase in heat, systolic blood pressure (SBP) decreased by 1.1 mmHg (95% CI: −1.6, −0.6) and diastolic by 0.3 mmHg (95% CI: −0.6, −0.1). Among non-users of anti-hypertensive medications, heat-associated decreases in SBP were 2.1 mmHg greater among individuals with central air conditioning vs. without. Confidence intervals around the remaining modifiers were wide after multiple-comparisons corrections or sensitivity analyses.

Conclusions: Outdoor heat is associated with decreasing blood pressure, and cardiovascular vulnerability may vary primarily by ownership of central air conditioning.

Keywords

blood pressure; heart rate; temperature; vulnerability

INTRODUCTION

Heat is associated with increased cardiovascular and respiratory mortality, respiratory and renal hospital admissions, emergency department visits, and ambulance calls[1]. Although most research on heat and health has focused on these severe health events, heat exposure likely results in measurable physiologic effects that precede severe events.

In small experiments with healthy volunteers subjected to heat stress, subtle cardiac responses to heat stress have been observed, including changes in heart rate and blood pressure[2]. These hemodynamic changes with temperature have also been seen in larger observational studies[3]. Reductions in blood pressure at rest and increases in heart rate are primarily normal cardiac responses that promote cooling by increasing blood flow to the skin. However, especially in individuals with underlying medical conditions, these responses could lead to adverse health effects. For example, individuals taking antihypertensive medications have increased rates of syncope in hot, dry summer months, likely due to low systemic blood pressure[4].

Several factors may increase vulnerability to the adverse health effects of heat. In studies of heat and heat waves, odds of mortality or heat stroke were increased among individuals who were unmarried, were living alone, or had little social contact[5]. Furthermore, persons with pre-existing cardiovascular, respiratory, or renal health conditions or diabetes are at increased risk of severe health events in response to heat exposures[5]. Other factors that modify the adverse effects of heat include use of certain medications and lack of air conditioning[5]. Lack of air conditioning may be a particularly strong risk factor for heat-associated mortality and morbidity, and the association between high temperature and mortality or hospitalization is reduced or absent in communities with high air conditioning prevalence[5–7]. To our knowledge, few large population-based studies have investigated how individual characteristics modify associations of heat exposure with early hemodynamic changes, and none of these studies have examined effect modification by air conditioning status[8–14].

In addition to individual-level characteristics, certain neighborhood characteristics have also been identified as changing vulnerability to summer heat. Vegetation likely reduces vulnerability by moderating temperatures in the surrounding area, and neighborhoods with more paved surfaces or higher satellite-derived surface temperatures experience more heat-related mortality and heat distress emergency calls[5]. Low levels of neighborhood safety might increase heat vulnerability, possibly by discouraging individuals from opening windows or traveling to cooler places[15]. Additionally, exposure to air pollution, including particulate matter, may increase heat vulnerability[16–21]. Mechanisms for these synergistic effects between air pollution and temperature are unclear but may involve pulmonary, cardiovascular, inflammatory, and autonomic changes related to air pollution exposure[22].

In a changing climate with increasing extreme heat events[23], it is important to understand the mechanisms by which heat affects health and who is most vulnerable to heat. This knowledge will allow better targeting of assistance during extreme heat and may also suggest interventions (such as modifications of the built environment), which could help individuals and communities adapt to climate change.

We used unique longitudinal data from the Multi-Ethic Study of Atherosclerosis (MESA) to confirm the associations of heat with three markers of cardiovascular health in this cohort and then to examine factors that may modify these relationships. We hypothesized that: 1) Higher mean temperature on the day of and the day before the clinical exam would be associated with increases in heart rate and decreases in systolic (SBP) and diastolic blood pressure (DBP), controlling for age, season, and daily air pollution exposure; 2) Associations between temperature and heart rate, SBP and DBP would be stronger among individuals not using anti-hypertensive medications compared to individuals on medication (given the potential for certain anti-hypertensive medications to suppress thermoregulatory responses); and 3) Among individuals not using anti-hypertensive medications, associations between temperature and heart rate, SBP and DBP would be stronger in persons with lower renal function, impaired fasting glucose, lower social support, lower air conditioning use, lack of central air conditioning, higher $PM_{2.5}$ exposure and higher NO_x exposure and in areas with less vegetation and safety.

METHODS

Health Outcomes Data

MESA enrolled 6814 white, African-American, Hispanic and Chinese participants aged 45–84 years who were free of cardiovascular disease between 2000 and 2002 (baseline exam). Individuals were enrolled from six sites: Forsyth County (Winston–Salem), North Carolina; New York, New York; Baltimore, Maryland; Minneapolis–St. Paul, Minnesota; Chicago, Illinois and Los Angeles, California. Individuals completed questionnaires and underwent a total of five physical exams in clinics from 2000–2010. Additional details are provided elsewhere[24]. Secondary analyses of these data were approved by the University of Michigan Institutional Review Board.

Study outcomes included heart rate, SBP and DBP, each measured at five exams. For each exam, heart rate and brachial SBP and DBP were taken in the seated position after a 5-

minute rest using a Dinamap automated oscillometric sphygmomanometer. The available measures for heart rate (one at the baseline exam and three each at exams 2–5) and blood pressures (three per exam) were averaged within each exam.

Exposure Data

The main exposure of interest was the mean temperature of the day before and the day of the MESA exam. Temperature data were obtained from the National Climatic Data Center for eight community stations, which were usually at airports, and assigned to each participant based on proximity and date of exam.

Key time-varying confounders included ozone, $PM_{2.5}$, age and long-term time trends. Daily $PM_{2.5}$ and ozone levels were obtained from the EPA Air Quality System from a single long-running monitor for each site. The 2-day mean of daily ozone and $PM_{2.5}$ were calculated to match the temperature averages. We replaced ozone values missing in months when ozone was not monitored with site-specific minima for Winston–Salem, NC (November-March, all exams), Baltimore, MD (November-March, exams 2–3) and Minneapolis–St. Paul, MN (October-March, exams 1–2).

Individual-level variables investigated as effect modifiers included exam-specific estimated glomerular filtration rate (eGFR, a measure of renal function estimated from creatinine), blood pressure medication use (yes/no), impaired fasting glucose status (≥6.1 mmol/L, <6.1 mmol/L) as an indicator of diabetes or pre-diabetes, body mass index (BMI), defined as kg/m^2 measured at each exam, and tertiles of self-reported total weekly moderate and vigorous physical activity. Participants' air conditioner ownership (central or other) and its typical use in July were surveyed via technician-administered questionnaire from exams 3–5. We derived emotional social support using an index that ranged from 6–30 and consisted of six 5-point Likert-scored items from a questionnaire[25]. Individual air quality measures investigated as effect modifiers were levels of oxides of nitrogen (NO_x) and particulate matter less than 2.5 μm in diameter ($PM_{2.5}$) within the previous 2 weeks, which were modeled at the participants' residence for each exam[26]. Note that the air pollution measures investigated as long-term effect modifiers, NO_x and $PM_{2.5}$, were specific to residential addresses but summarized over two weeks, whereas the air pollution measures included as potential confounders of short-term two-day temperature, i.e., ozone and $PM_{2.5}$, were averaged over two days and were from a single monitor for each site.

Neighborhood characteristics investigated as effect modifiers included vegetation, defined as median normalized difference vegetation index at 250m buffers around the home address, calculated from a series of 16-day composite satellite images from the year 2006. Neighborhood safety was measured using a safety scale, comprised of three items, each reported on a Likert-scale ranging from one (strongly agree) to five (strongly disagree). These three items were administered to MESA participants and a separate sample of community members. Reponses were aggregated using empirical Bayes estimation to obtain estimates at each exam for each tract, conditional on MESA site, gender, age and survey sample. Internal consistency and additional details have been described previously[27,28].

Statistical Methods

We used fixed effects models for cohort studies with repeated measures to estimate associations of temperature with our three outcomes[29]. In these models, commonly used in the field of economics, associations are estimated using only within-individual variability in the exposure and outcomes. This removes within-person correlation due to person-level responses and non-time-varying confounding by using fixed effects, or dummy variables, for each participant as opposed to random effects, which are assumed to be uncorrelated with the observed explanatory variables. Although main effects of time-invariant factors cannot be investigated, their interactions with temperature can be included, allowing investigation of effect modification.

No standard definition for “warm temperatures” or “extreme heat” exists. We modeled temperature exposure as a piecewise linear spline of 2-day mean temperature in degrees Celsius preceding each exam, with a single knot at the site-specific 75th percentile of daily mean temperature from 1981–2010. In exploratory analyses of the associations between temperature and each health effect in each city using natural cubic splines, the 75th percentile of temperature was identified as a reasonable knot choice. As has been used in similar study designs[30,31], sine and cosine terms for month-of-year, and interactions between these terms and site indicator variables, were included. This controls for intra-annual seasonal effects, given that certain cardiovascular measures, such as blood pressure, vary seasonally. The following sensitivity analyses were performed: 1) The sine and cosine terms were replaced with bimonthly indicator variables. 2) We used June-September data only, with monthly indicator variables. 3) We included an interaction between baseline age and time. 4) We included quadratic terms for baseline age and year and a cubic term for year to account for potential confounding by nonlinear age and time trends. 5) The knot for the temperature spline was set at the 90th percentile of daily mean temperature, a commonly used threshold for more extreme heat[6,32–36]. However, too few participants had exams on extreme-heat days for effect modification analyses at this threshold. 6) We excluded the 25% of individuals for whom we were missing information on at least one of the potential effect modifiers. 7) Finally, given that power plant emissions increase on hot days[37], ozone and particulate matter may mediate the temperature-health association[38,39]. Therefore, to measure the total effect of temperature on each outcome, we excluded these pollutants from the model.

Given the possibility that hypertension medications could affect response to temperature, *a priori*, all analyses were stratified by hypertension medication use within two weeks prior to the visit. Other potential effect modification was studied using interaction terms between the modifier of interest and the piecewise spline of the main effect. The time-varying effect modifiers, such as eGFR, were averaged over the follow-up period using available measurements to derive an estimate of the mean level. The means were then interacted with time-varying temperature, thereby estimating whether the associations of within-person deviations in temperature with within-person deviations in outcomes were modified by the person’s average covariate level, e.g. eGFR, over the follow-up period.

Effect modification by one factor (e.g. neighborhood factors) may be confounded by other correlated effect modifiers (e.g. air conditioning use) through complex causal pathways, so

the model-specific covariate sets were selected *a priori*. In examining effect modification by eGFR, we adjusted for impaired fasting glucose on the effect modification scale. Likewise, for impaired fasting glucose, we adjusted for BMI, BMI^2 and physical activity, but eGFR was considered a mediator and thus excluded. For the remaining covariates, we adjusted for all other individual and neighborhood potential effect modifiers and physical activity, BMI and BMI^2.

Using heart rate as an example outcome, the final model was of the form:

$$HR_{it} = \alpha_i + \beta_1 \sin(MOY_{it}) + \beta_2 \cos(MOY_{it}) + \beta_3 \sin(MOY_{it}) \times SITE2_i + \beta_4 \cos(MOY_{it}) \times SITE2_i + \ldots + \beta_{11} \sin(MOY_{it}) \times SITE6_i + \beta_{12} \cos(MOY_{it}) \times SITE6_i + \beta_{13} AGE_{it} + \beta_{14} OZ_{it} + \beta_{15} PM_{it} + \beta_{16} T_{<=75th,it} + \beta_{17} T_{>75th,it} + \beta_{18} SITE2_i \times T_{<=75th,it} + \beta_{19} SITE2_i \times T_{>75th,it} + \ldots + \beta_{26} SITE6_i \times T_{<=75th,it} + \beta_{27} SITE6_i \times T_{>75th,it} + \beta_{28} EM1_i \times T_{<=75th,it} + \beta_{29} EM1_i \times T_{>75th,it} + \ldots + \beta_{39} EM12_i \times T_{<=75th,it} + \beta_{40} EM12_i \times T_{>75th,it} + \varepsilon_{it}$$

Equation 1

For each participant *i* and day *t*, HR_{it} was heart rate and α_i was a participant-specific dummy variable. $SITE2_i$-$SITE6_i$ were site-specific dummy variables. MOY_{it}, $T_{<=75th,it}$, $T_{>75th,it}$, AGE_{it}, OZ_{it}, and PM_{it} were the month-of-year (standardized to have a period of 2π and centered at August), temperature at or below the 75th percentile for that site, temperature above the 75th percentile for that site ("warm temperatures"), age (identical to "year" in this design), 2-day mean ozone and 2-day mean $PM_{2.5}$ at exam day *t*, respectively. $EM1_i$-$EM12_i$ were the effect modifiers, each centered on the grand mean and standardized for increases in the grand interquartile range. Participants without that outcome measured on at least two occasions were dropped. Instead of conditioning on subject fixed effects, we used a de-meaning procedure [29], estimating deviations from the within-person means for each independent and dependent variable at each person–visit. This produced identical results but was computationally faster.

We examined variance inflation factors and outliers. We removed one participant's exam for the heart rate analysis for which the participant had an outlying resting heart rate of 186 bpm.

For the purposes of selecting notable interactions, we estimated a Benjamini-Hochberg corrected type 1 error rate of 0.0037 at a false-discovery rate of 0.10 to account for multiple (nine modifiers × three outcomes × two antihypertensive medication use strata) tests of effect modification. We also considered false-discovery rates of 0.2 and 0.3 for type 1 error rate of 0.0074 and 0.0222, respectively, as thresholds below which results were suggestive of effect modification. All analyses were performed in R version 3.0.1.

RESULTS

Of the 6,814 participants at baseline, 6,191 consented to the use of their residential addresses for neighborhood and/or air quality estimates. Complete data on hypertension status, daily

air pollution, and temperature and the outcome on at least two exams were available for 6,027 and 6,066 participants for heart rate and blood pressure, respectively. Of these, 4,533 and 4,555, respectively, had complete information on all effect modifiers for inclusion in effect modification analyses. The number of participants, person–visits (18,471 total), and person–visits on warm temperature days were similar across sites (Table S1). At most of the person–visits, the participant had not used anti-hypertensive medications in the previous two weeks, except in Winston–Salem, NC (eTable 1).

Winston–Salem, NC had the highest 75th percentile of temperature as well as the highest AC use and percentage of participants with central AC (91.4%, Table 1). The site with the lowest percentage of participants with central AC (8.0%) was New York City, NY. July AC use and two-day mean daily ozone were also highest in Winston–Salem, NC. Los Angeles, CA had the lowest AC use but the highest two-day mean daily $PM_{2.5}$ level. Mean normalized difference vegetation index ranged from 108.8 (Los Angeles, CA) to 194.1 (Winston–Salem, NC) and mean 2-week NO_x ranged from 14.7 ppb (Winston–Salem, NC) to 69.6 (New York City, NY). The outcomes and most of the other personal and neighborhood characteristics were similar across the sites. Most of the correlations among the within-person means of the potential effect modifiers were weak, although 2-week NO_x was moderately correlated with normalized difference vegetation index ($r = -0.59$) and 2-week $PM_{2.5}$ ($r = 0.38$). (Table 2). SBP and DBP were moderately correlated with each other ($r = 0.59$) but only weakly correlated with heart rate ($r = -0.04$ and 0.13, respectively).

We observed a decrease of 1.1 mmHg (95% confidence interval (CI): −1.6, −0.6) in SBP and 0.3 mmHg (95% CI: −0.6, −0.1) in DBP for each 2°C increase in warm temperature (Model 1, Table 3). These associations persisted when: including an interaction between baseline age and time in the model; controlling for season using bimonthly indicators instead of sine and cosine terms for month-of-year; restricting the model to June-September and using monthly indicator variables; defining warm temperature at the 90th rather than the 75th percentile threshold; and restricting the analysis to individuals for whom information was available for all the potential effect modifiers (Models 2–7, Table 3). Additionally, the total effect of warm temperature on SBP (−0.9 mmHg, 95% CI: −1.4, −0.5), as measured in model 8 which did not include air pollutants, was similar to the effects in model 1, which did include these terms (Table 3). The heat–SBP associations were slightly stronger among users of anti-hypertensive medications (−1.2 mmHg per 2°C) vs. non-users (−0.5 mmHg per 2°C), although the confidence intervals were wide. We did not observe an association between heart rate and warm temperature in any of the models in either category of anti-hypertensive medication use.

Although the overall association between SBP and warm temperature was slightly stronger among individuals taking anti-hypertensive medications, we found effect modification of this association by other factors only among individuals not taking anti-hypertensive medications (Figure part B). After a multiple-comparisons correction, we observed effect modification by central air conditioner ownership of the association between SBP and warm temperature in the direction opposite that hypothesized. Specifically, among individuals with central air conditioning who were therefore assumed to have less heat exposure, a 2°C increase in warm temperature was associated with a 1.4 mmHg decrease in SBP (95% CI:

−2.2, −0.5). Among individuals without central air conditioning, this effect was reversed (0.8mmHg, 95% CI: −0.2, 1.7), for an interaction effect of central air conditioning ownership of −2.1 mmHg of SBP (p = 0.0012). Results were similar when season was modeled as bimonthly indicator variables (eFigure 1). When including an interaction between baseline age and time (model 3), our effect modification results were virtually identical (results not shown). When restricting our analysis to individuals whose central air conditioner ownership status did not change over the course of the study, we also still found significant effect modification by central air conditioner ownership of the association between warm temperature and SBP (eFigure 2).

For heart rate, 2-week $PM_{2.5}$ modified the association between warm temperature and heart rate among anti-hypertensive medication users in model 1 in the direction hypothesized. Among these individuals whose home residences were at the 25th percentile of 2-week $PM_{2.5}$ exposure (12.2 μg/m^3), we observed a 0.3 bpm decrease in heart rate (95% CI: −0.9, 0.2) for a 2°C increase in warm temperature. In contrast, among individuals whose home residences were at the 75th percentile of 2-week $PM_{2.5}$ exposure (15.8 μg/m^3), we observed a 0.6 bpm increase in heart rate (95% CI: 0.2, 1.1) for a 2°C increase in warm temperature. However, this result was attenuated after multiple-testing correction; when we modeled season with bimonthly indicator terms; and when we excluded individuals whose 2-week $PM_{2.5}$ exposure varied greatly over the course of the study (eFigures 1 and 2).

Among anti-hypertensive medication non-users, results were suggestive of modification of the heat-heart rate and heat-blood pressure associations by eGFR and social support. Individuals with lower eGFR had responses in the direction of increased susceptibility to heat, as hypothesized. Specifically, these individuals had increased heart rate and decreased SBP or DBP in some of the models as compared to individuals with better renal function. For social support, among individuals with worse social support, results were opposite to those hypothesized. Specifically, among individuals with lower social support, SBP and DBP decreases with heat were attenuated. However, the eGFR and social support effect modification results were eliminated after multiple-hypothesis correction.

DISCUSSION

In this six-site U.S. study of associations between heart rate, blood pressure, and temperature, heart rate was not associated with heat, but our results confirmed findings from earlier studies that SBP is inversely associated with warm temperature[3,40,41], even when allowing for a potential non-linear association between SBP and temperature. However, our study was unique in having individual-level air conditioner ownership and use information. Among people without central air conditioning, one might expect the increased exposure to higher ambient temperatures on warm days to result in decreased SBP, but we observed the opposite effect. One explanation may be that for individuals without central air conditioning, entering an air-conditioned doctor’s office may result in a pronounced decrease in skin temperature and a transient increase in blood pressure, thereby offsetting the effects of warm outdoor temperatures. Another explanation is that individuals without central air conditioning may be better adapted to high temperatures and may therefore have less

pronounced decreases in blood pressure in response to warm temperatures as compared to individuals with air conditioning who are typically sheltered from this exposure.

The idea that physiologic adaptation to warm temperatures may differ by central air conditioner ownership is supported by a small study, which found that individuals generally exposed to air conditioned as opposed to non-air-conditioned environments had a weaker capacity for physiologic regulation in an artificial heat shock environment[42]. Although the inverse association between temperature and blood pressure is well documented, some studies have found that *nocturnal* blood pressure is actually increased when temperature is high, due perhaps to poor sleep quality[43,44]. The association between blood pressure and temperature exposure is complex, and further study of blood pressure responses to heat across a range of daytime and nighttime in-home temperatures is warranted.

Central air conditioner ownership was the only consistent modifier of the association between warm temperature and either heart rate, SBP or DBP. Other factors' effects were obscured after multiple-hypothesis adjustment or in sensitivity analyses. Results were suggestive of effect modification by social support, eGFR and $PM_{2.5}$, and previous studies have suggested increased vulnerability to heat among individuals who are socially isolated, with renal impairment and on days with higher air pollution levels[5,16–21]. However, we may lack the power to detect the more subtle effects of these other modifiers, which have been identified in previous studies as characteristics of vulnerability. For example, for SBP among nonusers of anti-hypertensive medications, the added effect of the interaction between warm temperature and social support was −0.77 (−1.42, −0.12) mmHg. The confidence interval width is inversely proportional to the square root of the degrees of freedom, so with several strong assumptions (e.g., the effect size and residual sum of squares remain constant with increasing sample size), we would need a total sample size of approximately 4,200 persons, or a 65% increase in sample size, to realize this social support effect at the multiple-hypothesis testing correction type 1 error rate of 0.0037. Nevertheless, our results are consistent with the idea that central air conditioning largely influences the effects of outdoor temperature on the cardiovascular system and suggest that lack of central air conditioning is a more important characteristic of vulnerability than the other characteristics tested.

A major strength of this study is that air conditioner ownership and use information were available at the individual level. Air conditioner use and ownership were moderately correlated with other potential characteristics of vulnerability. Studies that do not account for individual air conditioning exposure likely bias the estimated effects of other characteristics of vulnerability. This is a challenge for both research and practice, since individual air conditioner ownership information is usually not available. This finding also suggests that vulnerability maps, which often weight proxies of central air conditioner ownership, such as income, equally with other characteristics of vulnerability, such as vegetation, potentially misrepresent vulnerability to warm temperatures.

Limitations of this study include lack of information at all the visits on exam room temperature as well as indoor home temperature. However, indoor home temperature may be correlated with outdoor temperature, and outdoor temperature effects on measurements taken in a doctor's office may reflect dehydration due to earlier exposure to higher indoor

and/or outdoor temperatures. For patient confidentiality reasons, dates of exam were removed after matching participants to daily temperature and pollutant exposures, so we were limited to using month-of-year, instead of day-of-year, to control for seasonal effects in the analysis. Our control of seasonal effects may have additionally been limited by our simplified sine-cosine parameterization of seasonal effects, although the blood pressure-temperature associations were similar when seasonal effects were characterized using alternate methods. For study design and power reasons, we were also limited to assuming a constant level of each effect modifier across the entire follow-up period within each person rather than allowing the modifiers to vary within person over time. However, most of the results were not sensitive to excluding individuals with high within-person variation in the effect modifier of interest.

This study evaluated associations between short term temperature and cardiovascular function indicators in a unique, multi-ethnic, U.S. based cohort with detailed individual clinical information as well as estimates of air pollution exposure and other important neighborhood characteristics known to mark vulnerability to heat-related health problems. Associations between warm temperatures and several subclinical indicators of cardiovascular function lend credence to previous findings linking increased outdoor temperatures to other cardiovascular morbidity and mortality endpoints. The dominance of air conditioner ownership as a factor modifying vulnerability to these associations between heat and blood pressure strongly in the direction opposite to that hypothesized suggests a complex yet important interaction between outdoor temperature and blood pressure that warrants further investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments:

The authors thank the other investigators, the staff, and the participants of the MESA study for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org.

Sources of Financial Support: This research was funded by a University of Michigan Graham Sustainability Institute Dow Sustainability Fellowship; and a Michigan Institute for Clinical and Health Research Postdoctoral Translational Scholars Program Fellowship (National Center for Advancing Translational Sciences grant UL1TR000433); the NIOSH Education and Research Center at University of Michigan (T42 OH008455–09); the Michigan Center for the Study of Lifestage Exposures and Adult Disease (P30 ES017885); National Science Foundation grant 1520803. This research was supported by contracts HHSN268201500003I, N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168 and N01-HC-95169 from the National Heart, Lung, and Blood Institute, and by grants UL1-TR-000040, UL1-TR-001079, and UL1-TR-001420 from NCATS. This publication was developed under a STAR research assistance agreement, No. RD831697 (MESA Air), awarded by the U.S Environmental Protection Agency. It has not been formally reviewed by the EPA. The views expressed in this document are solely those of the authors and the EPA does not endorse any products or commercial services mentioned in this publication.

REFERENCES

1. Song XP, Wang SG, Hu YL, Yue M, Zhang TT, Liu Y, Tian JH, Shang KZ. Impact of ambient temperature on morbidity and mortality: An overview of reviews. Science of the Total Environment 2017;586:241–254. [PubMed: 28187945]
2. Smith CJ, Johnson JM. Responses to hyperthermia. Optimizing heat dissipation by convection and evaporation: Neural control of skin blood flow and sweating in humans Auton Neurosci 2016.
3. Wang Q, Li CC, Guo YF, Barnett AG, Tong SL, Phung D, Chu C, Dear K, Wang XM, Huang CR. Environmental ambient temperature and blood pressure in adults: A systematic review and meta-analysis. Science of the Total Environment 2017;575:276–286. [PubMed: 27750133]
4. Huang JJ, Desai C, Singh N, Sharda N, Fernandes A, Riaz IB, Alpert JS. Summer syncope syndrome redux. Am J Med 2015;128(10):1140–3. [PubMed: 26052028]
5. Gronlund CJ. Racial and socioeconomic disparities in heat-related health effects and their mechanisms: a review. Curr Epidemiol Rep 2014;1(3):165–173. [PubMed: 25512891]
6. Anderson GB, Bell ML. Weather-related mortality: A study of how heat, cold, and heat waves affect mortality in the United States. Epidemiology 2009;20(2):205–213. [PubMed: 19194300]
7. Gronlund CJ, Zanobetti A, Wellenius GA, Schwartz JD, O'Neill MS. Vulnerability to Renal, Heat and Respiratory Hospitalizations During Extreme Heat Among U.S. Elderly. Climatic Change 2016;136(3):631–645. [PubMed: 27453614]
8. Madaniyazi L, Zhou Y, Li S, Williams G, Jaakkola JJ, Liang X, Liu Y, Wu S, Guo Y. Outdoor Temperature, Heart Rate and Blood Pressure in Chinese Adults: Effect Modification by Individual Characteristics. Sci Rep 2016;6:21003. [PubMed: 26876040]
9. Chen Q, Wang J, Tian J, Tang X, Yu C, Marshall RJ, Chen D, Cao W, Zhan S, Lv J, Lee L, Hu Y. Association between ambient temperature and blood pressure and blood pressure regulators: 1831 hypertensive patients followed up for three years. PLoS One 2013;8(12):e84522. [PubMed: 24391962]
10. Lanzinger S, Hampel R, Breitner S, Ruckerl R, Kraus U, Cyrys J, Geruschkat U, Peters A, Schneider A. Short-term effects of air temperature on blood pressure and pulse pressure in potentially susceptible individuals. Int J Hyg Environ Health 2014;217(7):775–84. [PubMed: 24877761]
11. Kent ST, Howard G, Crosson WL, Prineas RJ, McClure LA. The association of remotely-sensed outdoor temperature with blood pressure levels in REGARDS: a cross-sectional study of a large, national cohort of African-American and white participants. Environ Health 2011;10(1):7. [PubMed: 21247466]
12. Barnett AG, Sans S, Salomaa V, Kuulasmaa K, Dobson AJ, Project ftWM. The effect of temperature on systolic blood pressure. Blood Pressure Monitoring 2007;12(3):195–203. [PubMed: 17496471]
13. Yang L, Li LM, Lewington S, Guo Y, Sherliker P, Bian Z, Collins R, Peto R, Liu Y, Yang R, Zhang YR, Li GC, Liu SM, Chen ZM, China Kadoorie Biobank Study C. Outdoor temperature, blood pressure, and cardiovascular disease mortality among 23 000 individuals with diagnosed cardiovascular diseases from China. European Heart Journal 2015;36(19):1178–U107. [PubMed: 25690792]
14. Lewington S, Li LM, Sherliker P, Guo Y, Millwood I, Bian Z, Whitlock G, Yang L, Collins R, Chen JS, Wu XP, Wang SJ, Hu YH, Jiang L, Yang LQ, Lacey B, Peto R, Chen ZM. Seasonal variation in blood pressure and its relationship with outdoor temperature in 10 diverse regions of China: the China Kadoorie Biobank. Journal of Hypertension 2012;30(7):1383–1391. [PubMed: 22688260]
15. Sampson N, Gronlund CJ, Buxton MA, Catalano L, White-Newsome JL, Conlon KC, O'Neill MS, McCormick S, Parker EA. Staying cool in a changing climate: Reaching vulnerable populations during heat events. Global Environ Chang 2013;23:475–484.
16. Burkart K, Canario P, Breitner S, Schneider A, Scherber K, Andrade H, Alcoforado MJ, Endlicher W. Interactive short-term effects of equivalent temperature and air pollution on human mortality in Berlin and Lisbon. Environ Pollut 2013;183:54–63. [PubMed: 23941745]

17. Ren C Does particulate matter modify the association between temperature and cardiorespiratory diseases?(Research). Environmental health perspectives 2006;114(11):1690. [PubMed: 17107854]
18. Cheng Y, Kan H. Effect of the interaction between outdoor air pollution and extreme temperature on daily mortality in Shanghai, China. J Epidemiol 2012;22(1):28–36. [PubMed: 22041530]
19. Analitis A, Michelozzi P, D'Ippoliti D, De'Donato F, Menne B, Matthies F, Atkinson RW, Iniguez C, Basagana X, Schneider A, Lefranc A, Paldy A, Bisanti L, Katsouyanni K. Effects of heat waves on mortality: effect modification and confounding by air pollutants. Epidemiology 2014;25(1):15–22. [PubMed: 24162013]
20. Li J, Yang J, Gao J, Gu S, Li J, Xu L, Liu X, Liu Q. Modification of the effects of air pollutants on mortality by temperature: A systematic review and meta-analysis. Science of the Total Environment 2017;575:1556–1570. [PubMed: 27780592]
21. Qin RX, Zhu Y, Xia J, Liu Q. The interactive effects between high temperature and air pollution on mortality: A time-series analysis in Hefei, China. Science of the Total Environment 2017;575:1530–1537. [PubMed: 28029451]
22. Gordon CJ. Role of environmental stress in the physiological response to chemical toxicants. Environmental Research 2003;92(1):1–7. [PubMed: 12706749]
23. IPCC. Summary for Policymakers In: Stocker TF, Qin D, Plattner G-K, Tignor M, Allen SK, Boschung J, Nauels A, Xia Y, Bex V, Midgley PM, eds. Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. United Kingdom and New York, NY, USA: Cambridge University Press, 2013.
24. Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, Greenland P, JacobsJr. DR, Kronmal R, Liu K, Nelson JC, O'Leary D, Saad MF, Shea S, Szklo M, Tracy RP. Multi-Ethnic Study of Atherosclerosis: Objectives and Design. American Journal of Epidemiology 2002;156(9):871–881. [PubMed: 12397006]
25. Mezuk B, Roux AVD, Seeman T. Evaluating the buffering vs. direct effects hypotheses of emotional social support on inflammatory markers: The Multi-Ethnic Study of Atherosclerosis. Brain, behavior, and immunity 2010;24(8):1294–1300.
26. Szpiro AA, Sampson PD, Sheppard L, Lumley T, Adar SD, Kaufman JD. Predicting intra-urban variation in air pollution concentrations with complex spatio-temporal dependencies. Environmetrics 2010;21(6):606–631.
27. Mujahid MS, Diez Roux AV, Cooper RC, Shea S, Williams DR. Neighborhood stressors and race/ethnic differences in hypertension prevalence (the Multi-Ethnic Study of Atherosclerosis). Am J Hypertens 2011;24(2):187–93. [PubMed: 20847728]
28. Mujahid MS, Diez Roux AV, Morenoff JD, Raghunathan TE, Cooper RS, Ni H, Shea S. Neighborhood characteristics and hypertension. Epidemiology 2008;19(4):590–8. [PubMed: 18480733]
29. Wooldridge JM. Econometric Analysis of Cross Section and Panel Data (2nd Edition). Cambridge, MA, USA: MIT Press, 2011.
30. Bhaskaran K, Gasparrini A, Hajat S, Smeeth L, Armstrong B. Time series regression studies in environmental epidemiology. Int J Epidemiol 2013;42(4):1187–95. [PubMed: 23760528]
31. Wilker EH, Yeh G, Wellenius GA, Davis RB, Phillips RS, Mittleman MA. Ambient temperature and biomarkers of heart failure: a repeated measures analysis. Environ Health Perspect 2012;120(8):1083–7. [PubMed: 22588803]
32. Wang J, Williams G, Guo Y, Pan X, Tong S. Maternal exposure to heatwave and preterm birth in Brisbane, Australia. Bjog 2013;120(13):1631–41. [PubMed: 24034563]
33. Gronlund CJ, Zanobetti A, Schwartz JD, Wellenius GA, O'Neill MS. Heat, heat waves and hospital admissions among the elderly in the United States, 1992–2006. Environ Health Perspect 2014;122(11):1187–1192. [PubMed: 24905551]
34. Zhang K, Rood RB, Michailidis G, Oswald EM, Schwartz JD, Zanobetti A, Ebi KL, O'Neill MS. Comparing exposure metrics for classifying 'dangerous heat' in heat wave and health warning systems. Environ Int 2012;46:23–9. [PubMed: 22673187]

35. Guo Y, Li S, Zhang Y, Armstrong B, Jaakkola JJ, Tong S, Pan X. Extremely cold and hot temperatures increase the risk of ischaemic heart disease mortality: epidemiological evidence from China. Heart 2013;99(3):195–203. [PubMed: 23150195]

36. Michelozzi P, Accetta G, De Sario M, D'Ippoliti D, Marino C, Baccini M, Biggeri A, Anderson HR, Katsouyanni K, Ballester F, Bisanti L, Cadum E, Forsberg B, Forastiere F, Goodman PG, Hojs A, Kirchmayer U, Medina S, Paldy A, Schindler C, Sunyer J, Perucci CA. High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. Am J Respir Crit Care Med 2009;179(5):383–9. [PubMed: 19060232]

37. Abel D, Holloway T, Kladar RM, Meier P, Ahl D, Harkey M, Patz J. Response of Power Plant Emissions to Ambient Temperature in the Eastern United States. Environmental Science & Technology 2017;51(10):5838–5846. [PubMed: 28466642]

38. Buckley JP, Samet JM, Richardson DB. Commentary: Does air pollution confound studies of temperature? Epidemiology 2014;25(2):242–5. [PubMed: 24487206]

39. Reid CE, Snowden JM, Kontgis C, Tager IB. The role of ambient ozone in epidemiologic studies of heat-related mortality. Environ Health Perspect 2012;120(12):1627–30. [PubMed: 22899622]

40. Crandall CG, Gonzalez-Alonso J. Cardiovascular function in the heat-stressed human. Acta Physiol (Oxf) 2010;199(4):407–23. [PubMed: 20345414]

41. Modesti PA. Season, temperature and blood pressure: A complex interaction. European Journal of Internal Medicine 2013;24(7):604–607. [PubMed: 23972926]

42. Yu J, Ouyang Q, Zhu Y, Shen H, Cao G, Cui W. A comparison of the thermal adaptability of people accustomed to air-conditioned environments and naturally ventilated environments. Indoor Air 2012;22(2):110–118. [PubMed: 21950966]

43. Brook RD, Shin HH, Bard RL, Burnett RT, Vette A, Croghan C, Williams R. Can Personal Exposures to Higher Nighttime and Early-Morning Temperatures Increase Blood Pressure? The Journal of Clinical Hypertension 2011;13(12):881–888. [PubMed: 22142347]

44. Modesti PA, Morabito M, Bertolozzi I, Massetti L, Panci G, Lumachi C, Giglio A, Bilo G, Caldara G, Lonati L, Orlandini S, Maracchi G, Mancia G, Gensini GF, Parati G. Weather-related changes in 24-hour blood pressure profile: effects of age and implications for hypertension management. Hypertension 2006;47(2):155–61. [PubMed: 16380524]

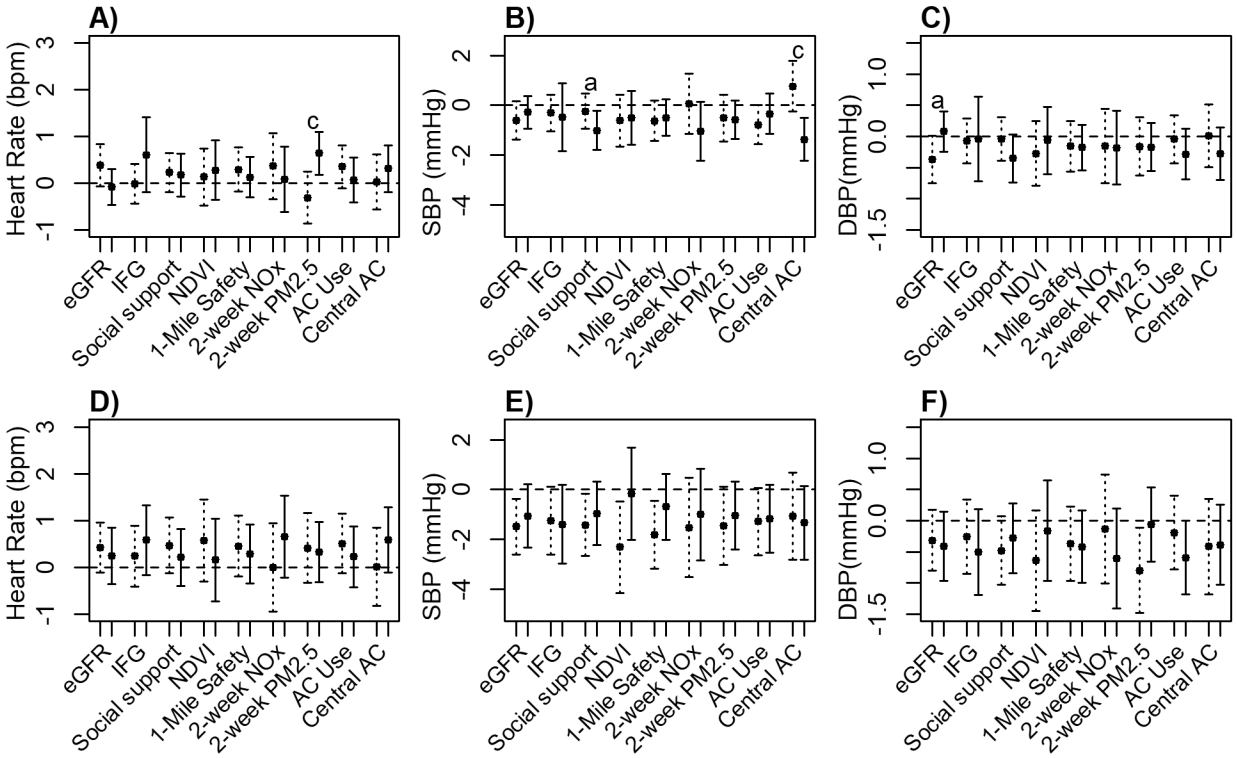

Figure.

Changes in heart rate, systolic (SBP) and diastolic blood pressure (DBP) for 2 °C changes in two-day mean temperature above the 75th percentile threshold, among individuals with high (75th percentile or present: ——) or low (25th percentile or absent: - - -) values of each characteristic, for exams during which individuals were not taking (A-C) or taking (D-F) anti-hypertensive medications. SBP = systolic blood pressure, DBP = diastolic blood pressure, PM2.5 = particulate matter less than 2.5 μm, BMI = body mass index, eGFR = estimated glomerular filtration rate, IFG = impaired fasting glucose, NDVI = normalized difference vegetation index, NOx = oxides of nitrogen, AC = air conditioning. Interactions notable for the following type 1 error rates: a: 0.0222, b: 0.0074, c: 0.0037. The terms interacted with temperature in each model were as follows: eGFR: eGFR, IFG; IFG: IFG, BMI, BMI^2; all other models: eGFR, IFG, social support, NDVI, 1-Mile Safety, 2-week NO_x, 2-week $PM_{2.5}$, AC Use, Central AC, Physical activity, BMI, BMI^2.

Table 1.

Percentages or means (standard deviations) of outcomes and exposures, across person-visits, overall and by site.

	Overall (N = 18,471)	Winston-Salem, NC (N = 3,364)	New York City, NY (N = 3,432)	Baltimore, MD (N = 2,848)	Minneapolis-St. Paul, MN (N = 2,021)	Chicago, IL (N = 3,897)	Los Angeles, CA (N = 2,907)
Outcomes[a]							
Heart rate (beats per minute)	64.4 (10.1)	64.1 (10.1)	65.5 (10.5)	64.0 (10.2)	63.8 (9.8)	64.9 (10.2)	63.6 (9.8)
SBP (mmHg)	123.9 (20.4)	128.8 (21.0)	123.2 (20.1)	124.0 (19.2)	121.0 (20.3)	121.5 (20.0)	123.8 (20.9)
DBP (mmHg)	70.0 (10.2)	70.9 (10.6)	71.1 (9.8)	69.8 (9.8)	69.3 (10.2)	69.6 (10.1)	69.1 (10.3)
Ambient Exposures[a]							
2-day mean ozone (ppb)	25.4 (10.7)	33.6 (10.0)	24.9 (10.5)	24.9 (11.4)	27.7 (9.9)	21.8 (9.7)	23.6 (8.9)
2-day mean $PM_{2.5}$ ($\mu g/m^3$)	14.6 (8.0)	14.2 (6.5)	13.9 (7.4)	15.3 (8.2)	9.9 (6.0)	15.7 (7.9)	17.2 (9.5)
Degrees above the 75th percentile (°C)[b]	0.7 (1.6)	0.6 (1.4)	0.8 (1.8)	0.6 (1.5)	0.9 (2.0)	0.8 (1.9)	0.4 (1.0)
Degrees above the 90th percentile (°C)	0.2 (0.7)	0.1 (0.5)	0.2 (0.8)	0.1 (0.5)	0.2 (0.7)	0.2 (0.7)	0.1 (0.5)
Personal and Neighborhood Exposures							
Hypertension medications[a]	45%	52%	47%	50%	39%	40%	42%
IFG[c]	32%	31%	35%	33%	30%	26%	36%
central AC[c]	61%	91%	8%	76%	53%	65%	72%
BMI (kg/m^2)[cd]	28.3 (5.4)	29.1 (5.4)	29.0 (5.4)	29.4 (5.3)	29.7 (5.2)	26.5 (4.9)	26.5 (5.0)
eGFR ($mL/min/1.73\ m^2$)[cd]	79.0 (16.4)	77.9 (16.6)	79.6 (16.4)	79.7 (16.4)	77.3 (16.7)	78.2 (15.3)	81.0 (17.3)
Social support index[cde]	24.3 (4.5)	24.9 (4.1)	23.9 (4.7)	24.9 (4.2)	24.3 (4.6)	23.4 (4.8)	24.5 (3.9)
NDVI[cd]	141.4 (40.8)	194.1 (13.7)	111.6 (23.7)	166.1 (30.8)	162.6 (14.5)	116.4 (31.4)	108.8 (15.3)
1-mile safety[cdf]	3.6 (0.4)	4.0 (0.3)	3.5 (0.3)	3.6 (0.3)	3.6 (0.3)	3.6 (0.4)	3.7 (0.2)
2-week NO_x (ppb)[cd]	38.7 (22.3)	14.7 (6.0)	69.6 (15.5)	32.4 (11.7)	21.4 (4.9)	35.3 (7.7)	53.5 (17.8)
2-week $PM_{2.5}$ ($\mu g/m^3$)[cd]	14.2 (2.7)	13.7 (1.3)	14.7 (2.3)	13.6 (1.7)	10.1 (1.2)	14.0 (1.6)	17.7 (2.6)
July AC use[cdg]	3.3 (0.9)	3.9 (0.4)	3.4 (0.9)	3.5 (0.8)	3.0 (0.9)	3.1 (0.9)	2.6 (0.9)

SBP = systolic blood pressure, DBP = diastolic blood pressure, $PM_{2.5}$ = particulate matter less than 2.5 μm, BMI = body mass index, eGFR = estimated glomerular filtration rate, IFG = impaired fasting glucose, NDVI = normalized difference vegetation index, NO_x = oxides of nitrogen, AC = air conditioning.

[a] See Supplemental Information Table S2 for the distributions of the deviations from the within-person means.

[b] 75th percentiles of temperature: 21.8 °C (New York City LaGuardia), 19.5 °C (New York City Westchester), 22.9 °C (Winston-Salem), 21.9 °C (Baltimore), 19.5 °C (Minneapolis-St. Paul), 22.2 °C (Los Angeles Riverside), 19.1 °C (Los Angeles Airport) and 20.1 °C (Chicago).

[c] Based on the within-person means across exams.

[d] Overall 25th-75th percentiles of the following characteristics: BMI: 24.6–31.3, EGFR: 68.3–89.1, Social support: 21.7–27.7, NDVI 250m: 105–177, 1-mile safety: 3.4–3.9, 2-week NO_x: 20.9–53, 2-week $PM_{2.5}$: 12.2–15.8, July AC use: 2.5–4.0.

[e]Range of 6–30, based on six 5-point survey questions, with higher values indicating more support.

[f]Survey safety scale: 1 = Strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree.

[g]July AC use scale: 1 = Not at all, 2 = A few days a month, 3 = More than half, 4 = Almost daily or thermostat.

Table 2.

Correlations[a] among the within-person means of the potential effect modifiers.

	BMI	eGFR	IFG	physical activity	social support	NDVI	1-mile safety	2-week NO_x	2-week $PM_{2.5}$	July AC use	Central AC
BMI	1										
eGFR	0.04	1									
IFG	0.29	0.07	1								
physical activity	−0.04	0.15	−0.08	1							
social support	0.00	−0.02	−0.01	0.02	1						
NDVI	0.00	−0.02	−0.03	0.04	0.05	1					
1-mile safety	−0.13	−0.10	−0.07	0.02	0.06	0.27	1				
2-week NO_x	0.03	0.01	0.03	−0.04	−0.05	−0.59	−0.28	1			
2-week $PM_{2.5}$	0.03	0.01	0.03	−0.02	−0.03	−0.28	−0.06	0.38	1		
July AC use	0.08	−0.01	0.04	−0.01	0.07	0.06	0.07	−0.06	−0.01	1	
Central AC	−0.07	−0.04	−0.05	0.01	0.08	0.14	0.27	−0.15	−0.06	0.13	1

SBP = systolic blood pressure, DBP = diastolic blood pressure, $PM_{2.5}$ = particulate matter less than 2.5 μm, BMI = body mass index, eGFR = estimated glomerular filtration rate, IFG = impaired fasting glucose, NDVI = normalized difference vegetation index, NO_X = oxides of nitrogen, AC = air conditioning.

[a]Pooled across sites.

Table 3.

Changes (95% confidence intervals) in heart rate, systolic (SBP) and diastolic blood pressure (DBP) for 2 °C increases in two-day mean temperature above the 75th or 90th percentile threshold, among individuals taking or not taking anti-hypertensive medications, overall for six models.

Anti-hypertensive medications	Model[a]	Heart rate (bpm) N = 6,027	SBP (mmHg) N=6,066	DBP (mmHg) N = 6,066
All	1	0.0 (−0.2, 0.3)	−1.1 (−1.6, −0.6)	−0.3 (−0.6, −0.1)
	2	0.0 (−0.2, 0.3)	−1.0 (−1.5, −0.6)	−0.3 (−0.6, −0.1)
	3	0.1 (−0.2, 0.3)	−1.1 (−1.6, −0.6)	−0.4 (−0.6, −0.2)
	4	0.1 (−0.2, 0.4)	−0.9 (−1.5, −0.4)	−0.3 (−0.6, 0.0)
	5	0.2 (−0.3, 0.6)	−1.4 (−2.2, −0.6)	−0.5 (−0.9, −0.1)
	6	−0.1 (−0.4, 0.3)	−0.9 (−1.6, −0.3)	−0.3 (−0.6, 0.0)
	7	0.2 (0.0, 0.5)	−1.0 (−1.6, −0.5)	−0.3 (−0.5, 0.0)
	8	0.0 (−0.2, 0.2)	−0.9 (−1.4, −0.5)	−0.3 (−0.5, −0.1)
No	1	−0.1 (−0.4, 0.3)	−0.5 (−1.0, 0.1)	−0.2 (−0.4, 0.1)
	2	−0.1 (−0.4, 0.3)	−0.4 (−1.0, 0.1)	−0.2 (−0.4, 0.1)
	3	0.0 (−0.3, 0.3)	−0.6 (−1.1, −0.0)	−0.2 (−0.5, 0.0)
	4	0.0 (−0.3, 0.4)	−0.4 (−1.0, 0.2)	−0.2 (−0.5, 0.1)
	5	0.1 (−0.4, 0.7)	−0.1 (−1.0, 0.8)	0.1 (−0.4, 0.5)
	6	−0.1 (−0.5, 0.3)	−0.2 (−1.0, 0.5)	−0.1 (−0.5, 0.2)
	7	0.1 (−0.3, 0.4)	−0.4 (−1.0, 0.2)	−0.1 (−0.4, 0.2)
	8	−0.0 (−0.3, 0.3)	−0.5 (−1.0, −0.1)	−0.3 (−0.5, −0.0)
Yes	1	0.1 (−0.4, 0.5)	−1.2 (−2.2, −0.3)	−0.3 (−0.7, 0.0)
	2	0.1 (−0.3, 0.5)	−1.3 (−2.2, −0.4)	−0.4 (−0.8, 0.0)
	3	0.1 (−0.3, 0.6)	−1.3 (−2.2, −0.4)	−0.4 (−0.8, 0.0)
	4	0.3 (−0.2, 0.7)	−0.9 (−2.0, 0.1)	−0.2 (−0.7, 0.2)
	5	0.6 (−0.2, 1.4)	−2.0 (−3.7, −0.4)	−0.5 (−1.2, 0.2)
	6	−0.0 (−0.6, 0.6)	−1.2 (−2.5, 0.1)	−0.4 (−0.9, 0.2)
	7	0.4 (−0.1, 0.9)	−1.4 (−2.4, −0.3)	−0.4 (−0.8, 0.1)
	8	0.1 (−0.3, 0.5)	−0.9 (−1.7, −0.1)	−0.2 (−0.6, 0.1)

Results are for an “average” site from models with mean-centered site terms. See Supplemental Information Table S3 for site-specific results for model 1.

a

Model 1: model in equation 1.

Model 2: Model 1 + baseline_age × time.

Model 3: Model 1 + age^2 + year^2 + year^3.

Model 4: Model 1 with bimonthly indicator variables instead of sine and cosine terms for month-of-year.

Model 5: Model 1, June-September only, with monthly indicator variables. N = 1,608 and N = 1,640 for heart rate and blood pressure, respectively.

Model 6: Model 1 with warm temperature threshold at 90th percentile of site-specific temperature instead of 75th percentile.

Model 7: Model 1 without the 25% of individuals missing at least one effect modifier. N = 4,533 and N = 4,555 for heart rate and blood pressure, respectively.

Model 8: Model 1 without daily PM10 or ozone.